AMINOSYN II IN DEXTROSE - dextrose hydrous, isoleucine, leucine, lysine acetate, methionine, phenylalanine, threonine, tryptophan, valine, alanine, arginine, aspartic acid, glutamic acid, histidine, proline, serine, n-acetyl-tyrosine and glycine injection, solution
HOSPIRA, INC.

NOTE: These solutions are hypertonic. See WARNINGS and PRECAUTIONS.

Nutrimix® Dual-chamber Flexible Container
The Upper Chamber Contains 500 mL of Aminosyn II 7% (An Amino Acid Injection)
The Lower Chamber Contains 500 mL of 10% Dextrose Injection, USP
R_x only

DESCRIPTION

Upper Chamber: Aminosyn II 7%, an amino acid injection, 500 mL.
Aminosyn II 7% is a sterile, nonpyrogenic solution for intravenous infusion. The formulation is described in the table below.
Lower Chamber: 10% Dextrose Injection, USP, 500 mL.
10% Dextrose Injection, USP is a sterile, nonpyrogenic, hypertonic solution of Dextrose, USP in water for injection. The table below indicates the characteristics of this solution.
The container must be used only after removing the clamp and thoroughly mixing the contents of the two chambers. The solution resulting from mixing the contents of the upper and the lower chamber will be 3.5% amino acids with 5% dextrose. Mixing the contents of the upper and lower chambers yields a concentrated source of amino acids and carbohydrate calories for intravenous infusion. Headspace contains Nitrogen gas. The composition of this admixture is described in the table below.

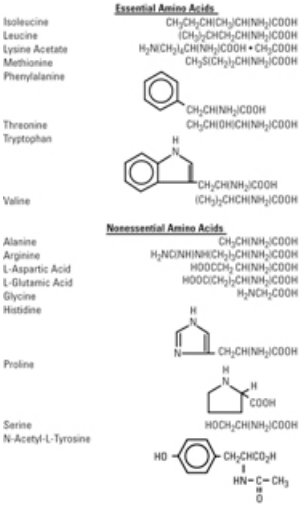
	Solution Composition per 100 mL		
	Upper Chamber	**Lower Chamber**	**Admixture**
Dextrose, hydrous (g)		10	5
Essential Amino Acids (mg)			
Isoleucine	462		231
Leucine	700		350
Lysine (as acetate salt)*	735		368
Methionine	120		60
Phenylalanine	209		104
Threonine	280		140
Tryptophan	140		70
Valine	350		175
Nonessential Amino Acids (mg)			
Alanine	695		348
Arginine	713		356
L-Aspartic Acid	490		245

L-Glutamic Acid	517	258
Histidine	210	105
Proline	505	252
Serine	371	186
N-Acetyl-L-Tyrosine	189	94
Glycine	350	175
Total Amino Acids (g)	7	3.5
Protein Equivalent (g)	7	3.5
Total Nitrogen (g)	1.07	0.54

*Amount cited is for lysine alone and does not include acetate salt.

	Upper Chamber	**Lower Chamber**	**Admixture**
Electrolytes (mEq/liter)			
Sodium [a] (Na^+)	36		18
Acetate [b] ($C_2H_3O_2^-$)	50.3		25.2
Sodium hydrosulfite added (mg/100 mL)	60.0		30.0
Osmolarity mOsmol/liter (actual)	647	546	585
pH	5.8	4.3	5.8
range	5.0 to 6.5[c]	3.2 to 6.5	5.0 to 6.5

The formulas for the individual amino acids are as follows:



[a] Includes sodium from the pH adjustor sodium hydroxide and the antioxidant, sodium hydrosulfite.

[b] Includes acetate from lysine acetate.

[c] May contain sodium hydroxide for pH adjustment.

Dextrose, USP is chemically designated D-glucose, monohydrate ($C_6H_{12}O_6 \cdot H_20$), a hexose sugar freely soluble in water.

The flexible plastic container is fabricated from a specially formulated nonplasticized thermoplastic co-polyester (CR3). Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly. Solutions inside the plastic container also can leach out certain of its chemical components in very small amounts before the expiration period is attained. However, the safety of the plastic has been confirmed by tests in animals according to USP biological standards for plastic containers.

CLINICAL PHARMACOLOGY

The Aminosyn II 3.5% in 5% Dextrose Injection admixture obtained upon mixing thoroughly the contents of the two chambers, provides carbohydrate calories and crystalline amino acids to promote protein synthesis and wound healing, and to reduce the rate of endogenous protein catabolism. This mixture given by peripheral vein with vitamins and maintenance electrolytes may be administered with intravenous fat emulsion to provide additional calories and prevent essential fatty acid deficiency.

INDICATIONS AND USAGE

Aminosyn II 3.5% in 5% Dextrose Injection infused through a peripheral vein is indicated as a source of nitrogen in the nutritional support of patients in whom for short periods of time oral nutrition cannot be tolerated, is undesirable or inadequate.

The addition of supplemental electrolytes will be required in accordance with the prescription of the attending physician.

CONTRAINDICATIONS

This preparation should not be used in patients with hepatic coma or metabolic disorders involving impaired nitrogen utilization.

WARNINGS

Parenteral infusion of amino acids, similar to the enteral ingestion of any protein, may induce a rise in blood urea nitrogen (BUN) especially in patients with impaired renal function. Appropriate laboratory tests should be performed periodically and the infusion eventually discontinued if BUN levels exceed normal postprandial limits and continue to rise. It should be noted that a modest rise in BUN normally occurs as a result of increased protein intake.

Administration of amino acid solutions to a patient with hepatic insufficiency may result in serum amino acid imbalances, metabolic alkalosis, prerenal azotemia, hyperammonemia, stupor and coma.

Solutions containing sodium ion should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency and in clinical states in which there exists edema with sodium retention.

Solutions which contain potassium ion should be used with great care, if at all, in patients with hyperkalemia, severe renal failure and in conditions in which potassium retention is present.

Solutions containing acetate ion should be used with great care in patients with metabolic or respiratory alkalosis. Acetate should be administered with great care in those conditions in which there is an increased level or an impaired utilization of this ion, such as severe hepatic insufficiency.

Aminosyn II 3.5% in 5% Dextrose Injection contains sodium hydrosulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Parenteral administration of amino acids may result in increased plasma ammonia concentration. Instances of asymptomatic hyperammonemia have been reported in patients without overt liver dysfunction. The mechanisms of this reaction are not clearly defined, but may involve genetic defects and immature or subclinically impaired liver function.
Hyperammonemia is of special significance in infants, as it can result in mental retardation. Therefore, it is essential that blood ammonia levels be monitored frequently in infants.
WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.
Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS
Special care must be taken when administering glucose solutions to provide calories in diabetic or prediabetic patients. To control and minimize possible hyperglycemia and consequent glycosuria, it is desirable to monitor blood and urine glucose and, if necessary, add insulin.
Because of its antianabolic activity, concurrent administration of tetracycline may reduce the nitrogen sparing effects of infused amino acids.
Feeding regimens which include amino acids should be used with caution in patients with history of renal disease, pulmonary disease, or with cardiac insufficiency so as to avoid excessive fluid accumulation.
Nitrogen intake should be carefully monitored in patients with impaired renal function.
Contains no more than 25 mcg/L of aluminum.

Pregnancy Category C.
Animal reproduction studies have not been conducted with Aminosyn II 3.5% in 5% Dextrose Injection. It is not known whether this admixture can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Aminosyn II 3.5% in 5% Dextrose Injection should be given to pregnant women only if clearly needed.

Geriatric Use
Clinical Studies of Aminosyn II in Dextrose Injection have not been performed to determine whether patients over 65 years of age respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. This drug is known to be substantially excreted by kidney, and the risk for adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Pediatric Usage
Due to their concentration, these solutions are not recommended for use in pediatric patients less than 1 year old. Frequent monitoring of serum glucose concentrations is required when dextrose is prescribed to pediatric patients, particularly neonates and low birth weight infants.
CLINICAL EVALUATION AND LABORATORY DETERMINATIONS, AT THE DISCRETION OF THE ATTENDING PHYSICIAN, ARE NECESSARY FOR PROPER MONITORING DURING ADMINISTRATION. Do not withdraw venous blood for blood chemistries through the peripheral infusion site, as interference with estimations of nitrogen containing substances may occur. Blood studies should include glucose, urea nitrogen, serum electrolytes, ammonia, cholesterol, acid-base balance, serum proteins, kidney and liver function tests, osmolarity and hemogram. White blood count and blood cultures are to be determined if indicated. Urinary osmolality and glucose should be determined as necessary.
Do not use unless the solutions are clear and container is undamaged. Discard unused portion.
Do not use if solution in either chamber is discolored or if clamp is open or missing.

ADVERSE REACTIONS
Aminosyn II 3.5% in 5% Dextrose Injection (without electrolyte additives) is hypertonic; it can be infused through a peripheral vein paying great care to the possible occurrence of local reactions. Local reactions consisting of a warm sensation, erythema, phlebitis and thrombosis at the infusion site have occurred with peripheral intravenous infusion of amino acids; in such cases the infusion site should be changed promptly to another vein. Use of large peripheral veins, inline filters, and slower rates of infusion may reduce the incidence of local venous irritation. Electrolyte additives should be spread throughout the day. Irritating additive medications may need to be injected at another venous site.
Generalized flushing, fever and nausea have been reported during peripheral infusions of amino acid solutions.

OVERDOSAGE

In the event of overhydration or solute overload, re-evaluate the patient and institute appropriate corrective measures. See WARNINGS and PRECAUTIONS.

DOSAGE AND ADMINISTRATION

The total daily dose of Aminosyn II 3.5% in 5% Dextrose Injection to be infused depends on the daily protein requirements and on the patient's metabolic and clinical response.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Peripheral Vein Nutritional Maintenance

Aminosyn II 3.5% in 5% Dextrose Injection is suitable for administration by peripheral vein. The solution is not intended for central vein infusion since it does not contain adequate amounts of amino acids or electrolytes for administration with high concentrations of dextrose.

For peripheral intravenous infusion, 1 to 1.5 g/kg/day of total amino acids will reduce protein catabolism. Infusion or ingestion of carbohydrate or lipid will not reduce the nitrogen sparing effect of intravenous amino acid infusions at this dose.

As with all intravenous fluid therapy, the primary aim is to provide sufficient water to compensate for insensible, urinary, and other fluid losses (nasogastric suction, fistula drainage, and diarrhea). Aminosyn II 3.5% in 5% Dextrose infused at a rate of 45 mL/kg/day, will meet the fluid and amino acid requirements of the stable adult patient.

As reported in the literature, the dosage and constant infusion rate of intravenous dextrose must be selected with caution in pediatric patients, particularly neonates and low birth weight infants, because of the increased risk of hyperglycemia/hypoglycemia.

The daily requirements of the stable, nonhypermetabolic adult patient in an acceptable weight range with restricted physical activity are approximately 30 kcal/kg of body weight, 1 to 1.5 g amino acid/kg, and 2500 to 3000 mL of fluids. Each gram of infused dextrose provides 3.4 kcal; each gram of infused fat provides 9 kcal. A 10% lipid emulsion contains 1.1 kcal/mL. Lipid emulsion can be administered to provide up to 3 g fat/kg/day, infused simultaneously with Aminosyn II 3.5% in 5% Dextrose Injection by means of a Y-connector located near the infusion site, using separate flow controls for each solution. Aminosyn II 3.5% in 5% Dextrose Injection should not be premixed with fat emulsion. If it is anticipated that re-institution of oral feedings cannot occur for a prolonged period of time, consideration should be given to starting a central venous feeding regimen.

Electrolytes and vitamins must be added to the solution, per the physician's prescription, to meet individual patient requirements. SERUM ELECTROLYTES SHOULD BE MONITORED AS INDICATED.

Electrolytes may be added to the nutrient solution as indicated by the patient's clinical condition and laboratory determinations of plasma values. Major electrolytes are sodium, chloride, potassium, phosphate, magnesium and calcium.

Vitamins, including folic acid and vitamin K are required additives. The trace element supplements should be given when long-term parenteral nutrition is undertaken.

Pediatric

Pediatric requirements for parenteral nutrition are constrained by the greater relative fluid requirements of the infant and greater caloric requirements per kilogram. A 3.5% amino acid solution is too concentrated for use in pediatric patients less than 1 year old, who generally require a 2.5% amino acid solution. However, older pediatric patients can receive Aminosyn II 3.5% in 5% Dextrose Injection. The suggested amino acid dosage level for children between 4 and 12 years of age is 2 g/kg/day; for 13 to 15 years of age, 1.7 g/kg/day; and for 16 years of age and above, 1.5 g/kg/day. Energy requirements for children between 1 and 7 years of age are approximately 75 to 90 kcal/kg/day; for children 7 to 12 years of age, 60 to 75 kcal/kg/day; and for ages 12 to 18 years, 30 to 60 kcal/kg/day. Energy intake may be supplemented with intravenous fat emulsion. In cases of malnutrition or stress, these requirements may be increased.

Supplemental electrolytes and vitamin additives should be administered as deemed necessary by careful monitoring of blood chemistries and nutritional status. Iron supplementation is more critical in the child than the adult because of the increasing red cell mass required by the growing child. Serum lipids should be monitored for evidence of essential fatty acid deficiency in patients maintained on fat-free TPN. Bicarbonate should not be administered during infusion of the nutritional solution unless deemed absolutely necessary.

To ensure the precise delivery of the small volumes of fluid necessary for total parenteral nutrition in children, accurately calibrated and reliable infusion systems should be used.

DRUG INTERACTIONS

Additives may be incompatible. Consult with pharmacist, if available. When introducing additives, use aseptic technique, mix thoroughly and do not store.

INSTRUCTIONS FOR USE

DO NOT USE IF AMINOSYN II IS DISCOLORED OR IF CLAMP IS OPEN OR MISSING. COLOR VARIATION IN THE DEXTROSE INJECTION FROM PALE YELLOW TO YELLOW IS NORMAL AND DOES NOT ALTER EFFICACY.

To Open:

Tear outer wrap at notch. After removing the overwrap, check for minute leaks by squeezing the container firmly. If leaks are found, discard solution as sterility may be impaired. If supplemental medication is desired, follow directions below before preparing for administration.

To Add Medication:

1. Prepare the appropriate additive port.
2. Using aseptic technique and an additive delivery needle of appropriate length, puncture resealable additive port at target area through inner diaphragm and inject. Withdraw needle after injecting medication.
3. The additive ports should be protected by covering with additive caps.
4. Mix container contents thoroughly.

Preparation for Administration
(Use aseptic technique)

1. Open clamp between the two chambers. Completely drain all the solution and air into the lower chamber. To achieve this, stretch the side wall of the emptied top chamber.
2. Close flow control clamp of administration set.
3. Remove cover from outlet port at bottom of container.
4. Insert piercing pin of administration set into port with a twisting motion until the set is firmly seated. **NOTE:** See full directions on administration set carton.
5. Suspend from hanger at top of container.
6. Squeeze and release drip chamber to establish proper fluid level in chamber.
7. Open flow control clamp to expel air from set. Close flow control clamp.
8. Connect to infusion catheter.
9. Regulate rate of administration with flow control clamp. Ensure that all solution and air are in the lower chamber when reading fluid levels.

WARNING: Do not use flexible container in series connections.

HOW SUPPLIED

Aminosyn® II 3.5% in 5% Dextrose Injection is supplied in a 1000 mL volume dual-chamber flexible container (List No. 7701). Aminosyn II 3.5% in 5% Dextrose Injection is obtained by opening the clamp separating the two chambers and mixing the contents of the upper chamber,
500 mL of Aminosyn II 7% and the lower chamber, 500 mL of 10% Dextrose Injection, USP.
Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (25°C); however, brief exposure up to 40° C does not adversely affect the product.
Avoid exposure to light.
To prevent breakage, handle cold or refrigerated (2°C to 8°C) co-polyester (CR3) containers with care.

 EN-0128 Printed in USA

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